

REMARKS

A. The Status of the Claims and the Amendments

Claims 1-12, 14-16, and 20-48 are pending, of which claims 7, 10, 11, 21-39, and 43-48 were previously withdrawn from consideration. Claims 13, 17-19, and 49-100 were previously canceled without prejudice. By the present amendment, claims 1 and 2 have been amended to more particularly define the Applicant's invention and to claim it with greater specificity. As amended, the amended claims are supported by the specification and the original claims. No new matter have been added. More specifically, a limitation "the peptide contains between 2 and 100 amino acid residues" added to claim 1 is disclosed in the original specification (page 9, lines 3-4). It is submitted that the amendments place the claims in condition for allowance. Entry of the amendments is respectfully requested.

B. First Rejection Under 35 U.S.C. § 103(a)

Claims 1-6, 16, 17, 20, and 40-42 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,543,158 to Gref et al. in view of the European patent document EP 0727225 to Quay, U.S. Patent No. 5,981,478 to Ruoslahti et al. and U.S. Patent No. 5,238,714 to Wallace et al. (page 3, first paragraph of the Final Office Action). The Applicants submit that claim 17 was previously canceled, and therefore, should not have been rejected. With regard to the other claims, the rejection is respectfully traversed on the following grounds.

It is settled law that to establish a *prima facie* case of obviousness, the following three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference as proposed by the Examiner; (2) there must be a reasonable expectation of success and (3) the prior art reference must teach or suggest all of the

claim limitations. MPEP § 2143. Applicants submit that the above criteria have not been met.

Gref et al. neither disclose nor suggest a composition comprising polymer particles that are modified by conjugation targeting peptides to the particles where “the peptide contains between 2 and 100 amino acid residues,” as required by claim 1, as amended. Instead Gref et al. disclose that antibodies or fragments thereof can be covalently attached to the particles (col. 3, lines 23-24), as well as proteins (col. 3, line 28). Specifically, the use of Fab or Fab₂ antibodies is disclosed (col. 3, line 25).

It is known that Fab and Fab₂ are very large protein moieties having molecular weight of hundreds of thousands daltons, and included many thousands amino acid residues. Other proteins mentioned by Gref et al. are also known to have generally high molecular weights. To contrast, the peptides recited in claim 1 as amended are at best oligomers having much lower molecular weight.

It is submitted that while there are certain similarities in the chemical structure of peptides and proteins, the Applicants have specifically distinguished between the two classes by separately defining them (see, page 9, lines 3-10) to emphasize that the proteins and the peptides cannot be substituted for one another in the context of the present application. Those skilled in the art will appreciate that big differences in the molecular weight will result in different chemical and physical properties of the polymer-targeting ligand conjugates. Therefore, while Gref et al. briefly disclose using antibodies or proteins, they provide neither suggestion nor motivation to use low molecular weight or oligomeric peptides for making the conjugate.

Each of Quay, Ruoslahti et al., and Wallace et al., as well as the combination thereof, fail to cure this deficiency. Indeed, both Quay and Ruoslahti et al. disclose using various peptide ligands (e.g., RGD) and shows that polymers can be conjugated to such ligands. However, Quay’s teachings are limited to contrast agents only (see, abstract) and the disclosure of Ruoslahti et al. is limited to teaching that some specific peptides

having the RGD sequence can effectively bind to certain integrins (see, col. 9, lines 63-64). With respect to Wallace et al., all that is disclosed is a synthetic procedure that can be used for conjugating amino acid esters to polymers that form microcapsules (example 3, col. 9, lines 39-56). While the teachings of Wallace et al. show that some ligands can be attached to the particles, there is nothing in Wallace disclosing or suggesting that peptides can be such ligands. Accordingly, neither Quay nor Ruoslahti et al. nor Wallace et al. nor a combination of these references provide any motivation or suggestion of using the conjugates that are disclosed in nanoparticles.

In view of the foregoing, even if Gref et al., Quay, Ruoslahti et al. and Wallace et al. are combined, the combination of these three references does not disclose or suggest every element of claim 1. It is therefore submitted that claim 1, is patentably distinguishable over Gref et al. in view of Quay, Ruoslahti et al., and Wallace et al. Each of claims 2-6, 16, 20, and 40-42, depends, directly or indirectly, on claim 1 and is considered patentable for at least the same reason. Withdrawal of the rejection and reconsideration are respectfully requested.

C. Second Rejection Under 35 U.S.C. § 103(a)

Claims 1-6, 8, 9, 12-17, 20, and 40-42 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,759,431 to Hunter in view of U.S. Patent No. 5,578,325 to Domb et al. and in view of Ruoslahti et al. (page 4, last paragraph of the Final Office Action). Again, the Applicants submit that the rejection does not apply to the previously canceled claim 17. The same applies to the previously canceled claim 13. As to the other claims, the rejection is respectfully traversed on the following grounds.

The requirements that need be satisfied to have a valid obviousness rejection are as discussed above. Hunter discloses drug delivery systems, including microcapsules encapsulating a drug, particularly for delivery of camptothecin (see, e.g., col. 15, line 20), but fail to describe polymer particles conjugated to peptides, where “the peptide contains

between 2 and 100 amino acid residues,” as required by claim 1, as amended. Each of Domb et al., and Ruoslahti et al., as well as the combination thereof, fail to cure this deficiency. Specifically, Domb et al. discuss various diblock copolymers and targeting ligands that can be attached to them (e.g., see example 1 and table 1, col. 15), but fail to teach or suggest that the ligands can be peptides recited in claim 1, as amended. Ruoslahti et al. teach what is described above, and as previously discussed, provides no motivation or suggestion of using the conjugates that are disclosed in nanoparticles.

Accordingly, even if Hunter, Domb et al., and Ruoslahti et al. are combined, the combination of these three references does not disclose or suggest every element of claim 1. It is therefore submitted that claim 1, is patentably distinguishable over Hunter, Domb et al., and Ruoslahti et al. Each of claims 2-6, 8, 9, 12, 14-16, 20, and 40-42, depends, directly or indirectly, on claim 1 and is considered patentable for at least the same reason. In view of the foregoing, withdrawal of the rejection and reconsideration are respectfully requested.

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CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

No fee is deemed to be due in connection with this response. However, if any additional fee is due, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896.

Respectfully submitted,



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